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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,082	09/07/2005	Guido Rasi	2697-116	6975

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EXAMINER	
KUDLA, JOSEPH S	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
06/24/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/519,082	RASI ET AL.	
	Examiner	Art Unit	
	JOSEPH S. KUDLA	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-22* is/are pending in the application.

4a) Of the above claim(s) *16-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/23/07, 7/14/07 and 12/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restriction

1. Applicant's election of Group I in the reply, filed on March 14, 2008, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the Restriction requirement, filed on March 14, 2008, the election has been treated as an election without traverse (MPEP § 818.03(a)). Accordingly, the subject matter now under consideration is drawn to claims 11-15.

Priority

2. This application claims priority of International Application PCT/US03/20829, filed June 30, 2003, which claims priority to Provisional Patent Application 60/391,969, filed June 28, 2002 is acknowledged.

Information Disclosure Statement

3. The Information Disclosure Statement (IDS) correspondences submitted by Applicant on February 17, 2006, June 23, 2006 and February 11, 2008 are acknowledged. The references have been reviewed to the extent each is a proper citation on a U.S. Patent.

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a

separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specifically, the instant specification contains references on pages 7 and 8 which were not provided in an Information Disclosure Statement and therefore have not been considered.

Abstract

5. The abstract of the disclosure is objected to because The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 12 recites the limitation "the administration". There is insufficient antecedent basis for this limitation in the claim.

Appropriate action is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 11 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Giuliani et al. (Thymosin-alpha1 regulates MHC class I expression in FRTL-5 cells at transcription level," 2000, Eur. J. Immunol., Volume 30, Pages 778-786 ad cited by Applicant).

Giuliani et al. teach an increase in the expression of MHC class I surface molecules (*i.e.*, antigens) in murine and human tumor cell lines when treated with thymosin-alpha1 (Abstract and page 783, column 2, paragraph 2). Giuliani et al. shows the enhanced expression of the tumor antigens treated with thymosin-alpha1 relative to a control (page 782, column 2, paragraph 1 and figure 9D on page 783).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 11 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rasi et al. ("Anti-tumor effect of combined treatment with thymosin alpha 1 and interleukin-2 after 5-fluorouracil in liver metastases from colorectal cancer in rats," 1994, Int. J. Cancer, volume 57, Pages 701-705 and cited by Applicant, hereinafter Rasi1), in view of Rasi et al. ("A new human tumor-associated antigen(TLP) is naturally expressed in rat DHD-K12 colorectal tumor cells," 2000, Int. J. Cancer, Volume 85, Pages 540-544, hereinafter Rasi2).

Rasi1 teaches Interleukin-2 (IL-2) increases lymphocyte cytotoxic activities at high doses (page 701, column 1, paragraph 2, sentence 3). Rasi1 teaches pretreatment with Thymosin alpha 1 (TA1) *in vitro* and *in vivo* potentiates IL-2 induced cytotoxic activity (page 701, column 2, paragraph 1, sentence 2). Rasi1 also teaches the combined therapy of TA1 plus IL-2 after 5-Fluorouracil (5-FU) induced a marked, early increase in cytotoxic T-cell activity in the BDIX rat inoculated with DHD-K12 colorectal

cancer cells (page 703, column 2, paragraph 2, last two sentences). Rasi1 teaches the combination of IL-2, where IL-2 is given in a low dose, with TA1 is effective (page 704, column 2, first paragraph, last sentence), thus alleviating the toxicity concerns of IL-2 (page 701, column 1, paragraph 2, last sentence).

Rasi2 teaches a human tumor-associated antigen (TLP) is naturally expressed in rat DHD-K12 colorectal tumor cells (Title). Rasi2 teaches immunization with TPL induces a specific CTL response against DHD-K12 cells (page 544, column 2, paragraph 3, sentence 1). Rasi2 teaches that TLP expressed in DHD-K12 cells may be one of the tumor antigens responsible for the immunogenicity of these cells (page 544, column 2, paragraph 3, sentence 2).

Because the addition of TA1 with a lower dosage of IL-2 resulted in an equally effective CTL activity as that of a high dose of IL-2, one of ordinary skill in the art at the time of the invention could infer that the TA1 was responsible for the increased CTL activity as taught in Rasi1. Couple this with the disclosure of that immunization of DHD-K12 cells with TPL induces a CTL activity in Rasi2 and it would have been obvious to one of ordinary skill in the art at the time of the invention, that added TA1 results in increased TPL expression in the DHD-K12 cells, thus rendering instant claims 11 and 15 obvious.

9. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giuliani et al. (Thymosin-alpha1 regulates MHC class I expression in FRTL-5 cells at

transcription level," 2000, Eur. J. Immunol., Volume 30, Pages 778-786 ad cited by Applicant) , in view of Favelli et al. (European Patent Application EP 0 433 765).

Giuliani et al. teach an increase in the expression of MHC class I surface molecules (*i.e.*, antigens) in murine and human tumor cell lines when treated with thymosin-alpha1 (Abstract and page 783, column 2, paragraph 2). Giuliani et al. shows the enhanced expression of the tumor antigens treated with thymosin-alpha1 relative to a control (page 782, column 2, paragraph 1 and figure 9D on page 783).

Favelli et al. teach the use of immunomodulants as synergistic agents of chemotherapeutics in tumor therapy in humans (Title and page 4, first sentence). Thymosin-alpha1 was administered at 1 mg subcutaneously (page 4, lines 15 and 16).

It would have been obvious to one of ordinary skill in the art at the time of the invention that the combination of increased expression of tumor antigens when the cells are treated with TA1 as taught in Giuliani et al., coupled with the use of TA1 as an immunomoduant in humans would render instant claims 11 and 12 obvious.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in

that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.). It would have been obvious to one of ordinary skill in the art at the time of the invention that the working ranges for the administration of TA1 would be no more than routine optimization. Therefore, no more than routine experimentation, such as the results of routine dose-titration experiments, would have been necessary for one of ordinary skill in the art to arrive at a dosage for administration, thus rendering instant claims 13 and 14 obvious.

No claims allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph S. Kudla whose telephone number is (571) 270-3288. The examiner can normally be reached on 9am - 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph S. Kudla/
Examiner, Art Unit 1611
May 20, 2008

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615